

The Role of Intravenous Immunoglobulin (IVIG) in Guillain-Barré Syndrome Treatment

Audry Devisanty Wuysang*

Department of Neurology – Faculty of Medicine, Hasanuddin University

Introduction

Guillain-Barre´ syndrome (GBS) is the major cause of acute neuromuscular.(Hughes RAC, 2007) The term GBS includes a set of clinical syndromes with a common pathophysiological basis; an acute inflammatory polyneuropathy with an autoimmune etiology. Although usually characterized by a progressive flaccid paralysis with areflexia a wide range of motor, sensory and autonomic symptoms could be seen. In general, the diagnosis is based on clinical criteria; nevertheless, the presence of suggestive findings in the complementary test as demyelinating changes in the nerve conduction studies (NCS) or albuminocytological dissociation in the cerebrospinal fluid (CSF), help to confirm the diagnosis. (Gonzales-Suarez I, 2013)

The worldwide incidence of GBS is reported to be 0.6-2.4 cases per 100,000 per year [8-15]. The classic form, the acute inflammatory demyelinating polyradiculoneuropathy (AIDP), is the most frequent subtype in Europe, which accounts for 90% of GBS cases. Other subtypes like the axonal forms or the Miller-Fisher syndrome (MFS) are less common. (Gonzales-Suarez I, 2013)

Main Features of GBS

The main features of GBS are rapid progressive bilateral and relative symmetrical weakness of the limbs with or without involvement of respiratory or cranial nerve-innervated muscles or sensory disturbances. Patients have decreased or absent tendon reflexes. Cerebrospinal fluid examination typically shows an increased protein level with a normal white cell count. Pain frequently occurs and may cause severe complaints. It often starts before the onset of weakness and therefore can lead to diagnostic difficulties. Electromyography (EMG) can be helpful in confirming the diagnosis in clinically difficult cases such as in patients with extreme pain. EMG is especially useful for subclassifying GBS into subgroups such as acute motor axonal neuropathy (AMAN) and acute inflammatory demyelinating polyneuropathy (AIDP).

**Staff in the Department of Neurology, Faculty of Medicine, Hasanuddin University
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Clinical Course of GBS

Rapidly progressive weakness is the core clinical feature of GBS. By definition, maximal weakness is reached within 4 weeks, but most patients reach it within 2 to 3 weeks. Thereafter, patients enter a plateau phase that ranges from days to several weeks or months. This phase is followed by a usually much slower and variable recovery phase. In Europe, about one-third of GBS patients remain able to walk ("mild patients"); about 25% of the GBS patients who are unable to walk ("severe patients") need artificial ventilation. This is predominantly due to weakness of the respiratory muscles. Despite standard treatment with intravenous immunoglobulin (IVIG) or plasma exchange (PE) treatment, about 20% of severely affected patients remain unable to walk after 6 months. Moreover, many patients remain otherwise disabled or severely fatigued. Even 3 to 6 years after onset, GBS has a great impact on social life and the ability to perform activities of daily life. Therefore, GBS remains a severe disease for which better treatments are required. (van Doorn PA, Ruts L, Jacobs BC, 2008)

Table 1. Disability Scale for GBS (Hughes RAC, 2007)

-
- | | |
|----|--|
| 0. | Healthy |
| 1. | Minor symptoms or signs of neuropathy but capable of manual work/ <i>capable of running</i> |
| 2. | Able to walk without support of a stick (<i>5 m across an open space</i>) but incapable of manual work/ <i>running</i> |
| 3. | Able to walk with a stick, appliance or support (<i>5 m across an open space</i>) |
| 4. | Confined to bed or chair bound |
| 5. | Requiring assisted ventilation (<i>for any part of the day or night</i>) |
| 6. | Death |
-

The original scale is shown in regular print (Hughes *et al.*, 1978) and subsequent modifications in *italics* (Plasma Exchange/Sandoglobulin Guillain-Barré Syndrome Trial Group, 1997).

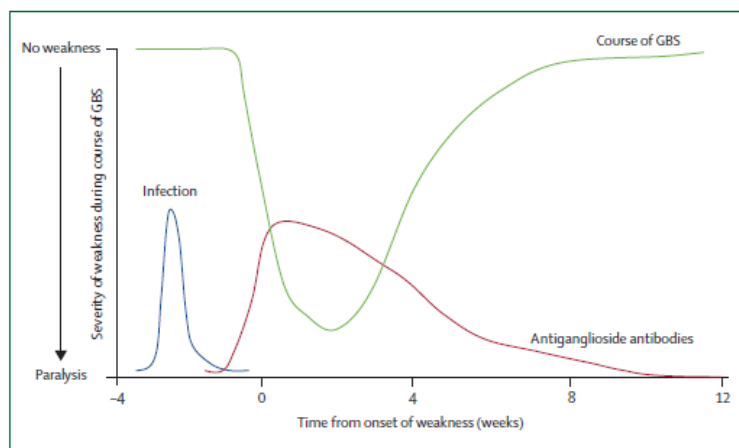


Figure 1: Relation between infections, antiganglioside antibodies, and clinical course of GBS

Immunobiology (van doorn, 2010)

AIDP is much more common than axonal forms in the Western world. Experimental evidence implicates autoantibodies to gangliosides as the cause of the axonal subgroups of GBS and of Fisher syndrome. These autoantibodies may be generated by the immune response to an infective organism, such as *Campylobacter jejuni*, cross-reacting with epitopes on the axon. The resemblance of AIDP to experimental autoimmune neuritis suggests pathogenetic mechanisms involving T-cell induced macrophage-associated demyelination. This proposed autoimmune aetiology led to the introduction of immunotherapy. Before its introduction, 10% of patients died and 20% were left seriously disabled. Plasma exchange (PE) was introduced as a possible treatment in 1978 and was shown to offer significant benefit by a randomized trial published in 1985. It became the gold standard against which other treatments were measured. (Hughes RAC, 2007)

There is convincing evidence that GBS at least in some patients is caused by an infection-induced aberrant immune response that damages the peripheral nerves. Four key factors were identified that control this process: (van Doorn PA, Ruts L, Jacobs BC, 2008)

1. Anti-ganglioside antibodies

In up to 50% of patients, serum antibodies to various gangliosides present in human peripheral nerves, including GM1, GD1a, GalNAc-GD1a, and GQ1b, can be demonstrated. Other antibodies may bind to mixtures or complexes of different gangliosides instead of individual ones. Interestingly, most of these antibodies are related to defined clinical subgroups of GBS.

2. Molecular mimicry and cross-reactivity

C. jejuni isolates from GBS patients express lipooligosaccharides (LOS) that mimic the carbohydrates of gangliosides. The type of ganglioside mimic in *C. jejuni* seems to determine the specificity of the anti-ganglioside antibodies and the associated variant of GBS. Antibodies in these patients usually are cross-reactive; they recognize LOS as well as gangliosides or ganglioside complexes. GBS after *Campylobacter* infection in anti-GM1/GD1a/GQ1b antibody-related cases is considered to be true example of molecular mimicry-related disease.

3. Complement activation

Postmortem studies demonstrated that local complement activation occurs at the site of nerve damage. A mice model for GBS showed that some anti-ganglioside antibodies are toxic for peripheral nerves and can cause blockade of nerve transmission and paralysis of the nerve-muscle preparation. Additionally, there is destruction of the nerve terminal and perisynaptic Schwann cells. Antibodies to GM1 affect the sodium channels at the nodes of Ranvier of rabbit peripheral nerves. All of these effects appear to be dependent on complement activation and formation of the membrane attack complex. The neurotoxic effects of these antibodies can be inhibited by IVIG and the complement inhibitor eculizumab.

4. Host factors

Less than 1:1,000 patients with a *C. jejuni* infection will develop GBS. Host factors may influence this susceptibility to develop GBS or the extent of nerve damage and outcome. Single nucleotide polymorphisms (SNPs) showed no consistent association with the susceptibility to develop GBS. Evidence indicates, however, that these SNPs may be important as disease-modifying factors. An association has been demonstrated between disease severity or outcome and SNPs in genes encoding for mannose-binding lectin, FcγRIII, MMP9, and TNF-α. However, confirmation in more extensive studies is required.

Table 2. Spectrum of GBS subtypes and serum antiganglioside antibodies

(van Doorn PA, Ruts L, Jacobs BC, 2008)

	Antibodies
Acute inflammatory demyelinating polyradiculoneuropathy (AIDP) ^{34,35,44,55}	Unknown
Acute motor (and sensory) axonal neuropathy (AMAN or AMSAN) ^{35,36,38,43,44,47,48,55,56}	GM1, GM1b, GD1a, GalNAc-GD1a
MFS and GBS overlapping syndrome ^{34,35,43,44,45,55}	GD3, GT1a, GQ1b
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Treatment of GBS

Treatment of GBS has two components: supportive care and specific therapy. Supportive care remains the cornerstone of therapy. If patients advance past the acute phase of illness, most will recover function. However, the neuropathy can advance so rapidly that endotracheal intubation and mechanical ventilation may be necessary within 24 hours of symptom onset. For this reason, all patients who have GBS should be admitted to a hospital for close observation for respiratory compromise, cranial nerve dysfunction, and autonomic instability. Autonomic nervous system dysfunction may manifest as fluctuations in blood pressure, cardiac dysrhythmias, gastrointestinal pseudo-obstruction, and urinary retention. Prophylaxis for deep venous thrombosis should be provided because patients frequently are immobilized for many weeks. As respiratory muscles weaken, elective endotracheal intubation should be considered. Progression to respiratory failure can be predicted using measurable respiratory parameters. Patients who are unable to demonstrate this minimal lung function require intubation. Frequent reassessment with serial lung function testing for rapid progression is critical. Additional predictors of subsequent mechanical ventilation include the following:

1. time from GBS onset to hospital admission of less than seven days,
2. inability to lift the elbows or head above the bed
3. inability to stand
4. ineffective coughing
5. increased liver enzyme levels

Predictors of mechanical ventilation in patients who had a previously determined vital capacity included time from GBS onset to admission of less than seven days, an inability to lift the head, and a vital capacity less than 60 percent predicted. One retrospective study²¹ demonstrated a 40 percent decrease from predicted vital capacity, compared with a 60 percent decrease reported in another study. This discrepancy may be related to different study methods and the larger number of patients enrolled in the latter study. Pain and psychologic stress should be treated. Narcotics should be used with caution because risk of ileus is already increased. Physical therapy, including gentle massage, passive range-of-motion exercises, and frequent position changes may provide pain relief. Carbamazepine and gabapentin have been used as adjuncts in pain management in GBS. Patients who were treated with these medications required less narcotic analgesia with fewer narcotic side effects and minimal sedation compared with those

who received placebo. Patients are paralyzed by the illness, but mentally alert and fearful. Reassurance and discussion about the phases of illness and recovery can help reduce psychologic stress.

Specific treatment should be initiated soon after diagnosis. High-dose intravenous immunoglobulin (IVIg; 400 mg per kg daily for five days) or plasmapheresis/plasma exchange (five exchanges over five to eight days) can be initiated. To determine whether IVIg was as effective as plasma exchange in treating patients with GBS, a large multicenter trial was designed to compare plasma exchange and IVIg and the combination of both treatments for GBS. The study followed 150 patients over four weeks. There were no statistically significant differences in the disability rating between the two treatment groups. IVIg and plasmapheresis were found to be equally effective therapies.

A. Use of Plasma Exchange in GBS

Therapeutic PE is an efficacious treatment option for patients with inflammatory neuropathies and is considered a first-line therapy in conditions such as AIDP. The basic mechanism for PE is the elimination of offending toxins or pathologic autoimmune antibodies from the bloodstream through extracorporeal separation from blood components. During PE, a patient's plasma and cells are separated through centrifugation or a filtration process. While the cells are reinfused into the patient, the plasma is replaced by a substitute fluid, usually albumin or fresh frozen plasma at a volume of 45 to 50 mL/kg. Plasma exchange requires two large bore access sites at alternate locations with a central line generally necessary due to the high flow volumes associated with treatment. Although effective, PE is invasive and can be time consuming, inconvenient, and overly burdensome to some. It also requires specialized personnel within an institutional setting who are able to run the necessary equipment. (Sederholm BH, 2010)

In addition to vascular access or technical complications, the use of PE may be further thwarted by troublesome or intolerable adverse reactions. Patients undergoing PE should be closely monitored for hypotension, infection, bleeding complications, and hypocalcemia. Chest pain, tachycardia, bradycardia, fever, rash, itching, nausea, vomiting, flushing, and dizziness may also occur in patients undergoing PE. More severe complications, including pulmonary embolism, sepsis, and anaphylactic shock have also been reported.

B. Use of IVIG in Immune-mediated Neuropathies (benson Sederholm, 2010, seminar in neurology)

IVIG is a first-line agent for the treatment of many neurologic disorders including chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), multifocal motor neuropathy (MMN), and GBS. The mechanism of action is not fully known, but it is thought to involve modulation of cellular and humoral immune system processes including antibody neutralization, complement attenuation, and the regulation of cytokine, B cell, and T cell activity. Therapeutic IVIG product is derived from the isolation of immunoglobulin from multiple human donor sources. The final product comes from a highly involved process involving plasma fractionation, purification, stabilization, and virus inactivation and removal. Commercially available IVIG products vary in how they are formulated and manufactured. Because of this, clinical impact is not insignificant and product differences should be considered when evaluating the clinical efficacy and safety of IVIG therapy for a given patient. Components to consider include volume load, infusion rate, osmolality, sodium content, sugar content, pH, and IgA content. Products with a higher sugar component may not be suitable for patients who are elderly, have diabetes, or at risk for renal dysfunction. Likewise products high in salt or osmolality may be a problem in patients with cardiac diseases, renal dysfunction, risk for venous thromboembolism, and in elderly or pediatric populations. As the incidence of adverse events may be related to patient characteristics, individualized products and their unique components should be evaluated judiciously. (Sederholm BH, 2010)

A potentially major problem with currently available IVIg preparations is the transmission of blood born pathogens, especially the non-A non-B (NANB) hepatitis of hepatitis C virus (HCV). It is difficult to estimate the risk of NANB infection following IVIg. The presence of HCV RNA (documented by PCR) in plasma pools prepared for anti-HCV negative units demonstrates the limitation of methods used to test plasma donations. In addition, the detection of HCV RNA in Cohn Fraction II prepared from these anti-HCV negative units and available data from patient treated with IVIg suggest that it is not possible to be sure that any of the products made until recently is completely free of NANB hepatitis. Thus, further procedures capable of maximizing the inactivation of NANB hepatitis are crucial for the increased safety of IVIg. One example of such method is the solvent detergent (S/D) treatment of plasma and its derivatives, which has been proven to result in HcV inactivation. Thus, an S/D virus inactivated IVIg preparation is likely to be HCV-free. Octagam® is an S/D virus inactivated IVIg with a physiologically distributed IgG subclass

and half life of 28 ± 3 days in primary hypogammaglobulinemic patients and 21 ± 3 days in Chronic Lymphocytic Leukemia patients. (Brenner 1996)

Table 3. Intravenous Immunoglobulin Product Comparison (Sederholm BH, 2010)

Product	Labeled Indication	Available Doses	Product Form	Half-life (days)	IgG Content	IgA Content	Sodium Content	Osmolality	Sugar Content	pH	Infusion Rate	Filtration
Carimune NF (CSL Behring LLC, Kankakee, IL)	PID ITP	3, 6, 12 gram vials	Lyophilized powder	21	$\geq 96\%$	720 $\mu\text{g/mL}$	<20 mg per gram of protein	192-1074 mOsm/kg based upon diluent and concentration	1.67 grams of sucrose per gram of protein	6.4-6.8	Initial: 0.5 mg/kg/min Titrate as tolerated to maintenance infusion of 3 mg/kg/min	Not required
Flebogamma 5% DIF (Grifols Biologicals Inc., Los Angeles, CA)	PID	0.5, 2.5, 5, 10, 20 gram vials	Liquid	30-45	$\geq 97\%$	<50 $\mu\text{g/mL}$	<3.2 mEq/L	240-370 mOsm/L	5 g/100 mL D-sorbitol	5.0-6.0	Initial: 0.5 mg/kg/min Titrate as tolerated to maintenance infusion of 5 mg/kg/min	Recommended 15-20 micron
Gammagard liquid 10% (Baxter Healthcare Corporation, Westlake Village, CA)	PID	1, 2.5, 5, 10, 20 gram vials	Liquid	35	98%	Average 37 $\mu\text{g/mL}$	Not detected	240-300 mOsmol/kg	None	4.6-5.1	Initial: 0.8 mg/kg/min Titrate as tolerated to maintenance infusion of 8.9 mg/kg/min	Not required
Gammagard S/D (Baxter Healthcare Corporation, Westlake Village, CA)	PID ITP KS CLL	2.5, 5, 10 gram vials	Lyophilized powder	37.7	90%	<1 $\mu\text{g/mL}$ in 5% solution	8.5 mg/mL	636 - 1250 mOsm/L based upon concentration	5%; 20 mg/mL glucose	6.4-7.2	Initial: 0.5 mL/kg/h Titrate as tolerated to maintenance rate of 4 mL/kg/h (8 mL/kg/h for 10% solution)	Required 15 micron
Gamunex (Talecris Biotherapeutics, Inc., Research Triangle Park, NC)	PID ITP CIDP	1, 2.5, 5, 10, 20 gram vials	Liquid	35	98%	Average 46 $\mu\text{g/mL}$	Trace	258 mOsmol/kg	None	4.0-4.5	Initial: 1-2 mg/kg/min Titrate as tolerated to maintenance infusion of 8 mg/kg/min Initial: 0.5 mg/kg/min Titrate as tolerated to maintenance infusion of 3.33 mg/kg/min	Not required
Octagam 5% (Octapharma USA Inc., Hoboken, NJ)	PID	1, 2.5, 5, 10, 25 gram vials	Liquid	40.7	96%	≤ 0.2 mg/mL	≤ 30 mmol/L	310-380 mOsmol/kg	100 mg/mL maltose	5.1-6.0	Initial: 0.5 mg/kg/min Titrate as tolerated to maintenance infusion of 3.33 mg/kg/min	Not required
Privigen 10% (CSL Behring LLC, Kankakee, IL)	PID ITP	5, 10, 20 gram vials	Liquid	36.6	98%	≤ 25 $\mu\text{g/mL}$	Trace	240-440 mOsmol/kg	None	4.6-5.0	Initial: 0.5 mg/kg/min Titrate as tolerated to maintenance infusion of 4-8 mg/kg/min	Not required

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The primary component of IVIG is immunoglobulin G, which is responsible for its therapeutic effects. The usual effective dose of IVIG for inflammatory neuropathies is 2 g per kg body weight, typically divided over 2 to 5 days. The rationale for this dose was initially based upon earlier studies of patients with idiopathic thrombocytopenia. The optimal dose of IVIG for neurologic disorders is not conclusively known. Following IVIG infusion, immunoglobulin G rapidly distributes within the intravascular and extravascular compartments with a peak serum concentration typically seen within 72 hours of infusion. Although serum levels of IVIG are generally not measured, a recent pharmacokinetic study of IVIG in AIDP patients suggested that the change in serum immunoglobulin G levels may be predictive of therapeutic responses. The half life of IVIG is ~20 days and immunoglobulins are primarily cleared in the plasma. Dosing of IVIG is typically done using total body weight. For obese patients (>100 kg), many clinicians use an adjusted body weight based upon IVIG pharmacokinetics.

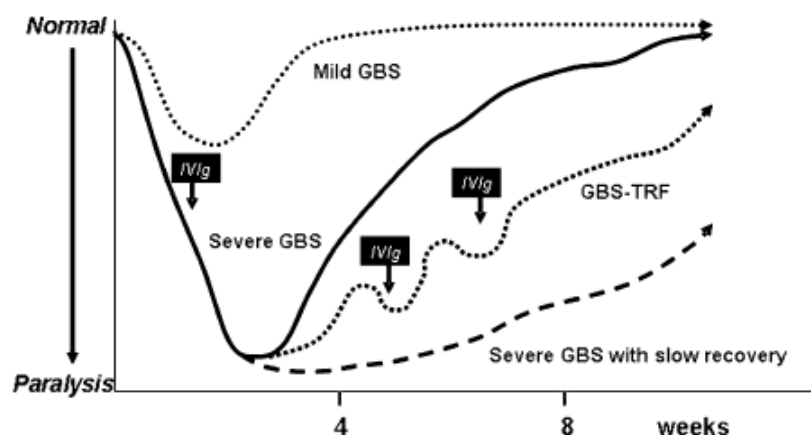


Figure 2. Variations in course of disease in GBS. Indicated are the courses of disease in mildly and severely affected GBS patients. The effect of IVIG in GBS has only been investigated in randomized controlled trials in patients unable to walk unaided at nadir (severely affected patients) and not in mildly affected patients (able to walk unaided at nadir). Whether mildly affected GBS patients may also benefit from IVIG is yet unknown. GBS patients who initially improve or stabilize after IVIG and subsequently deteriorate again have a “treatment-related fluctuation” (GBS-TRF): a condition that usually responds to an additional IVIG dose. Some GBS patients have a severe course of disease and a slow recovery phase. The prognosis of GBS patients can be determined using the Erasmus GBS Outcome Scale. Whether a second IVIG dose is effective in patients with a poor prognosis is not known yet

IVIG is generally well tolerated. Common adverse reactions include chills, fever, headache, fatigue, rigors, tremor, nausea, myalgias, malaise, and infusion-related reactions. More serious adverse events occur less frequently and include anaphylaxis, aseptic meningitis, acute renal failure, and venous thromboembolism. All patients receiving IVIG should have their

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vital signs checked at least every 15 minutes during the first hour of infusion and periodically thereafter. Surveillance for tolerability and adverse events should be done judiciously with each infusion session. Pretreatment with acetaminophen, antihistamines, such as diphenhydramine, or corticosteroids may help prevent or minimize adverse events. Markers of renal function should be monitored before each IVIG infusion and periodically thereafter. Appropriate chemical or physical prophylaxis for venous thromboembolism is also warranted. Too rapid rate of infusion may contribute to the incidence of adverse effects. Typically, IVIG infusions are initiated at a slow rate and increased based upon patient tolerability. At any point during an infusion the rate can be decreased to improve tolerability. In general, patients with renal dysfunction should have their rate of infusion decreased by one half of the normal infusion rate. IVIG is expensive and its availability may be limited in some centers. The clinical decision to use IVIG over alternative therapies should be done on an individualized basis and include such factors as pregnancy, disease severity, patient comorbidities, and tolerability.

Plasma Exchange vs IVIg in GBS

IVIg was introduced for GBS in 1988. In 1992, the first randomized trial comparing IVIg and PE showed similar effects from each treatment. Corticosteroids were introduced for GBS in the early 1950s. The first randomized trial, of ACTH, published in 1976 did not show a significant effect but the most recent trial reported possible minor short-term benefit when high dose intravenous methylprednisolone was combined with IVIg. The significance of this benefit has been debated. (HughesRAC, 2007)

Table 4. Common Adverse Reactions and Complications during administration of PE and IVIG

Summary of Plasma Exchange and Intravenous Immunoglobulin in the Management of Guillain-Barré Syndrome/Acute Inflammatory Demyelinating Polyradiculoneuropathy		
Interventional Regimen	Common Adverse Reactions	Severe Complications
Plasma exchange 5 treatments over 7 to 14 days	Hypotension, arrhythmias, infection, malaise, fever, flushing, dizziness, hypocalcemia	Pneumothorax, hemorrhagic complications, sepsis, thromboembolism, anaphylaxis
Intravenous immune globulin 0.4 g/kg daily for 5 days	Headache, myalgia, chills, fever, nausea, vomiting, fatigue, tremor, infusion site reactions	Acute renal failure, thromboembolism, aseptic meningitis, myocardial infarction, anaphylaxis

Clinical trials comparing IVIG to PE indicate equal benefit between the two treatment options in GBS. A Cochrane systematic review of six clinical trials found no difference in the change of disability scores with IVIG compared with PE at 4 weeks (RR = 1.09; 95% CI: 0.94-1.27). Other nonsignificant differences between IVIG and PE included no difference in the time needed to recover unassisted walking and the time until discontinuation of ventilator support in severe AIDP patients. This review also found that patients treated with IVIG tended to have fewer adverse events, fewer treatment complications, and were less likely to discontinue therapy as compared with PE. Complications with PE included infection, thrombosis, and hypotension. The largest trial in the systematic review included 383 severe AIDP patients who were randomized to receive IVIG 0.4 g/kg daily for 5 days, a course of five plasma exchanges administered over 8 to 13 days, or a combination of a 5-day course of PE followed by a 5-day course of IVIG therapy. All patients received interventions within 14 days of symptom onset. For the primary outcome of mean improvement in disability score at week 4 from randomization, no difference was observed between treatment groups. Combination therapy was not superior to IVIG or PE alone. Study authors suggested that due to the convenience of IVIG administration, as compared with PE, it represents a more favorable treatment option in the bulk of circumstances. A Quality Standards Subcommittee of the American Academy of Neurology endorsed IVIG as equivalent therapy to PE for AIDP patients. Combination therapy with PE and IVIG was not recommended. The Subcommittee further recommended that IVIG be used promptly within 2 to 4 weeks of disease onset in severe AIDP patients unable to walk without assistance. The usual IVIG treatment regimen is 0.4 g/kg given daily for 5 days. For patients with inadequate response or who relapse following IVIG administration, a repeat course of IVIG may be beneficial. (Sederholm BH, 2010)

Prognosis

Approximately 85 percent of patients with GBS achieve a full and functional recovery within 6 to 12 months. Recovery is maximal by 18 months past onset. However, some patients have persistent minor weakness, areflexia, and paresthesia. Approximately 7 to 15 percent of patients have permanent neurologic sequelae including bilateral footdrop, intrinsic hand muscle wasting, sensory ataxia, and dysesthesia. (Newswanger DL, Warren CR, 2004)

Death rate is described to be between 1-18%. (González-Suárez I et al, 2013) The mortality rate is less than 5 percent in tertiary care centers with a team of medical professionals who are familiar with GBS management. Causes of death include adult respiratory distress

syndrome, sepsis, pulmonary emboli, and cardiac arrest. Several factors during the acute phase of illness predict subsequent poor recovery. These factors include age older than 60 years; severe, rapidly progressive disease; and low nerve conduction amplitudes on distal stimulation, which suggests axonal loss.

In addition, prolonged mechanical ventilation for more than one month and preexisting pulmonary disease predict a poor outcome. In general, a poor long-term prognosis is directly related to the severity of the acute episode and delay in onset of specific treatment. Relapse occurs in a small percentage of patients. One multicenter trial¹⁸ of 229 patients showed a relapse rate of 3 to 5 percent. In that study, the relapse rate was not significantly affected by treatment type or any other factor tested.

Conclusions

In GBS patient, the administration of IVIG is thought to involve modulation of cellular and humoral immune system processes including antibody neutralization, complement attenuation, and the regulation of cytokine, B cell, and T cell activity.

Current treatment guidelines recognize PE and IVIG as equally efficacious agents for the treatment of GBS/AIDP. Both agents are clinically proven to hasten the time to recovery and improve disability scores when administered within the early stages of disease progression.

Patients treated with IVIG tended to have fewer adverse events, fewer treatment complications, and were less likely to discontinue therapy as compared with PE. Because of this, along with its ease of administration, IVIG is often recommended over PE therapy.

Combination therapy was not superior to IVIG or PE alone, thus are not recommended.

For patients with only mild forms of AIDP, few data are available to clarify the role of PE and IVIG. Despite effective therapies and supportive measures, residual functional deficits may persist in approximately one third of patients who experience AIDP.

A Quality Standards Subcommittee of the American Academy of Neurology endorsed IVIG as equivalent therapy to PE for AIDP patients. The Subcommittee further recommended that IVIG be used promptly within 2 to 4 weeks of disease onset in severe AIDP patients unable to walk without assistance.

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